-----Original Message-----
From: Allen, Samie Niver [mailto:SXN@CDRH.FDA.GOV]
Sent: Wednesday, December 22, 2004 1:13 PM
To: 'Free, Donna'
Subject: FW P030053/a5 - postapproval study issue

-----Original Message-----
From: Michael, Maher [mailto:MMichael@mentorcorp.com]
Sent: Tuesday, October 05, 2004 6:07 PM
To: 'Allen, Samie Niver'
Cc: Free, Donna
Subject: RE: P030053/a5 - postapproval study issue

Samie

Here is the modified response, along with the modified patient letter, and investigator agreement amendment. This response now answers the issue that number 4 response should address the Core Gel Study Investigators and subjects. If you have any questions, please do not hesitate to call.
Thanks

Mack

-----Original Message-----
From: Allen, Samie Niver [mailto:SXN@CDRH.FDA.GOV]
Sent: Tuesday, October 05, 2004 11:05 AM
To: 'Free, Donna'
Cc: Michael, Maher
Subject: P030053/a5 - postapproval study issue

Donna,

In your response to item 4 in your 9/30/04 email, you gave me a response that applies more to the general dissemination of the approved patient labeling/package labeling to new doctors and patients. My issue is with respect to the investigators and patients that will continue as part of your ongoing Core Study. There will be new information available and both the investigators and patients should be made aware of it. I believe that this is best accomplished by giving them a copy of the new labeling as an attachment to the Investigator Agreement and informed consent addenda. Unless you can propose an alternative means, please modify those 2 documents to state that you are providing them with a copy of the approved labeling so that they are aware of the dataset upon which the approval was based.

Thanks,
Samie

Further response to 23 Sep 2004 email from FDA, Clarifying that Study Sites and Subjects will receive Copies of Approved Labeling

4. Dissemination of the approved patient labeling/package labeling to the investigators and patients.

4 Response:
Mentor will provide a hardcopy of the approved patient labeling/package labeling to each Core Gel Study Investigator. Additionally, Mentor will provide each study site with enough hardcopies to disseminate to all study subjects. At their first exam after approval of the Mentor Silicone Gel-Filled Breast Implants, each of the study subjects will receive a copy of the approved patient labeling. Additionally, Mentor will post the updated patient labeling/package labeling on its website. We know that FDA will post this same information, along with other relevant breast implant related documents on the FDA website.

The letter that the patient signs, affirming that they are aware of the change in status for the Core Gel Study has been modified, to include an affirmation that the patient has received a copy of the approved patient labeling.

The amendment to the Investigator Agreement has also been modified, so that with her/his signature, s/he is affirming receipt of the patient labeling/package labeling and dissemination of the patient labeling to the Core Gel Study subjects.

Both of these documents are included with this response. The areas modified have been highlighted in yellow.

Response to 23 Sep 2004 email from FDA regarding Core Gel Postapproval Study

You stated that you do not believe that a separate postapproval study is necessary. However, FDA does not agree with this. While you may be proposing no change in the data collection, there is a different purpose to a postapproval study than a premarket study. Investigators and patients need to know that there has been a status change but that the study continues. Therefore, please provide a draft postapproval study that includes the following:

1. An Investigator Agreement addendum that states the purpose of the postapproval study and requires signature of the investigator. This will better assure that the investigators are well aware of the change in status of your device yet the continued required patient follow-up.

1 Response:
An addendum to the Investigator Agreement has been developed and is included in this response. This addendum explains that the Mentor Silicone Gel-Filled Breast Implants have been approved by FDA and the Core Gel study has been converted to a postapproval study. Each Investigator will sign the addendum, retain a copy for his/her study files, and send a copy to Mentor. .

2. If there are any protocol changes, then a description of any changes and copies of any revised CRFs. You should consider incorporating some level of follow-up on patients who have all devices removed with no replacement, rather than discontinuing these patients. You should also consider whether or not you need to modify the monetary incentives to keep investigators/patients after PMA approval.

2 Response:
No changes will be made to the Core Gel protocol. Mentor does not believe that it is necessary to follow patients after all study devices are explanted, as available data indicate that there are no health consequences associated with intact or ruptured implants. Moreover, it is unlikely that patients who no longer are implanted with Mentor devices would be willing to return for follow-up visits.

Mentor thinks that Investigator and subject monetary incentives are adequate (see the subject compensation table below). We will closely monitor subject follow up rates, and will revisit this issue if the follow up rates decrease significantly.

Subject Compensation for Years 4 Through 10

Visit	Payment
4 year visit	$150.00
5 year visit	$150.00
6 year visit	$150.00
7 year visit	$150.00
8 year visit	$150.00
9 year visit	$150.00
10 year visit	$150.00
Total	$1,050
Total + bonus*	$1,300

* If subject misses no postoperative visits, she receives a bonus of $250

3. An Informed Consent addendum that states the purpose of the postapproval study and requires signature of the patient. A description of any changes to the types of follow-up visits, monetary incentives, etc. should be described.

3 Response:
At their first exam after approval of the Mentor Silicone Gel-Filled Breast Implants, each subject will be given a letter that explains the status of the clinical study they have been participating, and the conversion of the status to pre-approval versus post-approval. The purpose of the postapproval study will be stated and the patients will be reminded of their commitment to continue to come back for all postoperative exams through ten years. Each subject will sign the letter, attesting that she received a copy. The original signed letter will be kept in the subject's study files and a copy will be sent to Mentor. A copy of the letter is included in this response.

4. Dissemination of the approved patient labeling/package labeling to the investigators and patients.

4 Response:
After Mentor Silicone Gel-Filled Breast Implants are approved, the updated labeling will be included in each gel implant packaged by Mentor that will be shipped to the physicians. Mentor will also make available at physician offices approved copies of the Patient Informed Decision Brochure. Additionally, Mentor will post the updated patient labeling/package labeling on its website. We know that FDA will post this same information, along with other relevant breast implant related documents on the FDA website.

Date

Dear Core Gel Study Patient:

It is my pleasure to inform you that the Mentor Silicone Gel-Filled Breast Implant(s) with which you were implanted were recently approved by FDA for commercial distribution in the United States. This means that doctors can now provide these silicone gel-filled breast implants as an option to any woman who desires them, without participation in a clinical study.

This approval would not have been possible without your commitment to the study. Your compliance with the protocol and returning for all the postoperative visits allowed us to provide FDA with detailed information about how these implants perform once implanted. Without your contribution, Mentor would not have received approval and these implants would not be an option for all women to consider.

While we do have approval for these breast implants, your commitment to this study is not yet done. The Core Gel Study is now considered a "postapproval study." We will continue to collect the same safety and effectiveness data that we did during the first years of the study. As you will recall, when you signed the original Core Gel Study informed consent, you agreed to return for yearly visits for ten years. We ask you to continue honoring this commitment. This is one of the important ways that we can gather long-term data on our silicone gel-filled breast implants and provide these additional data to FDA and you. Of course we will continue to compensate you for your time, paying $150 to you each time you return for your yearly postoperative exam. Additionally, if you are part of the MRI Substudy, please continue to return for these scans at 4, 6, 8, and 10 years after your original surgery date. The information from the MRI Substudy has been very instrumental in revealing the rupture rate of our implants.

The attached patient labeling goes over the results of the Core Gel Study. This information is also available on our website at Mentorcorp.com, FDA's website at FDA.gov, or you may call Mentor at 1-800- MENTOR8 for this information.

Thank you again for your past commitment to this study, and I will thank you in advance for your continuing involvement.

Regards,

Mentor

By my signature below, I am acknowledging that I received the letter from Mentor informing me that the Mentor Silicone Gel-Filled Breast Implant(s) with which I am implanted has been approved, and that I received a copy of the approved patient labeling, which contains the results of the Core Gel Study.

_____ _____

Patient Signature Date

_____

Patient name printed

Pat ID: _____ _____ _____

Site # Subject # Subject Initials

Attachment C
Addendum to Core Gel Study Investigator Agreement
Sponsor: Mentor, 201 Mentor Drive, Santa Barbara, CA USA 93111

Investigator:

This appends the Investigator Agreement for the Core Gel Study, between Mentor Corporation (Sponsor) and _____, M.D. (Investigator).

Effective insert date, FDA has approved Mentor's Silicone Gel-Filled Breast Implants for commercial distribution. Due to this approval, the Core Gel Study has been converted to a postapproval study. While the Core Gel Study is now a postapproval study, all aspects of the Core Gel Study protocol remain in-force, including but not limited to, bringing subjects back for all remaining postoperative follow-up visits and insuring that MRI Substudy subjects return for their MRI scans.

While all complications should continue to be reported as described in the Core Gel protocol, as this is now an approved device, they should also be reported via Medical Device Reporting (MDR) as defined in 21 CFR, part 803.

With your signature, you are stating that you understand that Mentor's Silicone Gel-Filled Breast Implants have been approved by FDA for commercial distribution, that all aspects of the Core Gel Study protocol remain in effect, and that you will not only report all complications as described in the Core Gel Study protocol, but also report these complications via MDR. Your signature also attests that you received copies of the approved patient labeling/package labeling, and will disseminate the patient labeling to your Core Gel study patients at their next exam.

Signatures

_____ _____
Investigator Signature Date

_____ _____
Cliff Kline, Program Director Date
Clinical Submissions
Mentor